Transplantation of Gene-Corrected Autologous CD34+ Hematopoietic Stem Cells in Previously Transplanted Patients with JAK3 Deficiency and Persistent Humoral Immune Defects

PIs: Sorrentino, Cunningham, and Buckley

NON-TECHNICAL ABSTRACT

Severe combined immunodeficiency (SCID) weakens the immune system in such a way that results in increased susceptibility to a wide variety of infections. Patients can be treated by transplanting normal blood stem cells obtained from a parent, brother, or sister. While transplantation fully corrects the immune system in more than half of the patients, about half who receive stem cells from their parents will have low levels of infection-fighting antibodies in their blood. As a result, these patients remain partially susceptible to infections and require regular intravenous treatments with expensive antibody preparations that are potentially contaminated with human viruses. In this protocol, we will treat such patients using a gene therapy approach. While SCID can be caused by a variety of defective genes, we will focus on those patients having abnormalities in the Janus 3 Kinase (JAK3) gene. We will obtain stem cells from either the blood or the bone marrow of the patient and introduce the JAK3 gene using a disabled mouse virus. Similar virus vectors have been used in human gene therapy procedures without any adverse effects. After infusing cells that have been exposed to the JAK3 virus, patients will be monitored both for potential side effects and for any evidence that the gene therapy procedure has improved their ability to make antibodies. Our hope is that this procedure will restore the patient's ability to make antibodies, and will allow them to discontinue regular intravenous antibody replacement. We also hope that this protocol will allow us to gain general knowledge regarding gene therapy approaches for human immunodeficiency diseases.